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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,874	02/06/2001	Iris Pecker	01/21603	8407

7590 01/26/2005

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,874	PECKER ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-67,71,72,76-78 and 80-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-67,71,72,76-78 and 80-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment of the specification and claims 64-66, 71, 72, 76-78, cancellation of claims 70, 73-75 and 79, and the addition of claims 80-113, in the paper of 11/8/2004, is acknowledged.

Claims 64-67, 71, 72, 76-78 and 80-113 are still at issue and are present for examination.

Applicants' arguments filed on 11/8/2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 64-67, 72, 76-78, 80-90 and 96-113 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly amended and added claims 64-67, 72, 76-78, 80-90 and 96-113 are rejected under this statute because the recited limitations, "consisting essentially of" and "is purified close to homogeneity" are not supported by the original specification at the time of filing and are thus considered new matter.

Claims 64-67, 71, 72, 76-78 and 80-113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein or preparation comprising said protein having the amino acid sequence of SEQ ID NO: 10, said protein having heparanase activity or being so cleavable so as to acquire said heparanase activity, does not reasonably provide enablement for any protein or preparation comprising said protein having heparanase activity or being so cleavable so as to acquire said heparanase activity, wherein said protein is merely 70% homologous to SEQ ID NO: 10 or a portion thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was made in the previous office action as it applied to previous claims 64-67 and 70-79. In response to this rejection applicants have amended claims 64-66, 71, 72, 76-78, cancelled claims 70, 73-75 and 79 and the added claims 80-113 and traverse the rejection as it applies to the new claims.

Applicants traverse this rejection as it applies to the newly amended and added claims on the basis that the claims in question are enabled by the disclosure, when filed, on the basis that while complex experimentation may be necessary, it is not

undue, as the nature of the art typically engages in such complex experimentation. Applicants note that that one of ordinary skill in the art would have been able to make and use the polypeptide of SEQ ID NO: 10, as stated previously and above. Applicants then submit that in addition one of skill in the art would have been able to modify the polypeptide of SEQ ID NO: 10 in order to form the other proteins within the scope of claim 64, having or being so cleavable to have heparanase activity.

While the enablement of the polypeptide of SEQ ID NO: 10 and the ability of one of ordinary skill in the art to modify such a protein is not in question, what is in question and continues to be found not enabled is the vast scope of those polypeptide encompassed by the currently claimed genus of polypeptides, including any polypeptide which consists essentially of a polypeptide at least 70% homologous to SEQ ID NO: 10 or to a portion thereof. It is noted for the record that the same arguments were made previously for those polypeptides merely 90% homologous to SEQ ID NO: 10 or to a portion thereof, and that with applicants previous amendment applicants have changed the scope of the claimed proteins from 90% homologous to SEQ ID NO: 10 to 70% homologous to SEQ ID NO: 10. While it is admitted that certainly one of skill in the art would have been able to make and use certain species encompassed by the current claims, it remains whether one of skill in the art would be able to make and use the vast majority of claimed polypeptides.

As previously acknowledged, while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing such variants as claimed by applicants (i.e., having or

being so cleavable as to have heparanase activity) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the multitude of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite number of possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish those characteristics which are necessary to enable such a broad genus as previously stated (i.e. (A) regions of the protein structure which may be modified without effecting heparanase catalytic activity; (B) the general tolerance of heparanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a heparanase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful).

Applicants continued submission, that applicant has submitted alignment data showing the homology between human, rat, mouse and chicken heparanase sequences as well as important shared features is acknowledged. While this information is helpful in enabling the claimed genus, by itself it appears to be insufficient to do such.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

with the scope of the claims broadly including any number of amino acid modifications of any heparanase having a mere 70% homology to SEQ ID NO: 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 64-67, 71, 72, 76-78 and 80-113 are rejected under 35 U.S.C. 102(b) as being anticipated by Fuks et al. (U.S. Patent No. 5,362,641).

The rejection was originally stated in the previous office actions, 10/21/2003, 7/1/2003 and 12/17/2003. In response to this rejection applicants have amended claims 64-66, 71, 72, 76-78, cancelled claims 70, 73-75 and 79, and added new claims 80-113 and traverse the rejection as it applies to the new claims. Newly added claims 80-113 are included in the rejection for the same reasons previously stated for claims 64-67 and 70-79. Further it is noted that the protein taught by Fuks et al. anticipates those claims drawn to recombinant heparanase, even though Fuks et al. may not specifically

teach production of the protein recombinantly. While the reference does not specifically disclose the enzyme produced by recombinant production (as recited by the claims), the production of a protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants continue to traverse along many of the lines of argument presented in the previous office action(s).

Applicants continued arguments that Fuks et al. failed to obtain pure heparanase is not found persuasive because applicants current claims "purity limitation(s)" continue to be anticipated by Fuks et al. as further discussed below. Applicants argue and submit the declarations of Dr. Pecker and Dr. Vlodavsky in support of applicants position that one of skill in the art would not consider that preparation taught by Fuks et al. "isolated heparanase protein".

Applicants argument that the antibodies raised in Fuks in an attempt to prepare anti-heparanase antibodies were actually anti-PAI-1 antibodies is acknowledged, however, as has been the position of the office, though not 100% pure, the preparation taught by Fuks et al. is that of "an isolated heparanase", from the same source as applicants claimed heparanase protein, and thus Fuks et al. anticipates applicants claimed "isolated heparanase protein" for all of the reasons of record.

Applicants further traverse the rejection on the basis that specifically with respect to claims 76 and new claim 107, one of ordinary skill in the art would not consider the "mixture of proteins" taught by Fuks et al. as "purified close to homogeneity" as now recited in these claims. This argument is acknowledged and can be appreciated, however, is found non-persuasive as it is somewhat unclear as to what one of ordinary skill in the art would consider "close to homogeneity" as opposed to what one of ordinary skill in the art would consider "homogeneous". Thus those claims reciting such a limitation continue to be anticipated by Fuks et al. because while applicants present evidence that the protein composition taught by Fuks et al. was not "homogeneous", it remains to be shown if that composition taught by Fuks et al. was not "close to homogeneity". Applicant is reminded that the office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re

Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants further argue with respect to claims 66 and 97 that in the claimed preparation comprising a protein component, the protein component must consist essentially of heparanase protein and applicants argue that Fuks et al. does not teach a preparation in which the protein component consists essentially of heparanase protein.

This argument is acknowledged and like that above can be appreciated, however is also found non-persuasive for similar reasons as the above argument. While applicants present evidence that the protein composition taught by Fuks et al. contained some impurities, it remains to be shown if that composition taught by Fuks et al. did not consist essentially of heparanase protein. Applicant is again reminded that the office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants is again reminded that an "isolated heparanase" like "An isolated heparanase " does not preclude the presence of potentially additional contaminating proteins.

Thus applicants argument has been considered in full and found to be non-persuasive.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Remarks

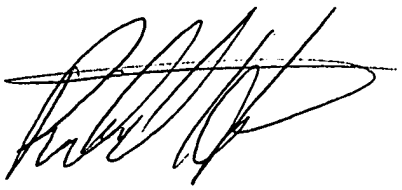
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
1/20/2005